HEPATITIS B – ACUTE AND CHRONIC *(initial diagnosis only)*; SURFACE ANTIGEN + PREGNANT WOMEN

DISEASE REPORTING

In Washington

DOH receives approximately 100 to 150 reports of acute hepatitis B virus (HBV) infections per year, for an average rate of 2.7/100,000 persons. Chronic hepatitis B and HBV surface antigen (HBsAg) carriage in pregnant women became reportable in 2000. There is usually one death each year associated with fulminant acute HBV infection.

Purpose of reporting and surveillance

- To identify sources of transmission (e.g., an infected health care worker or a contaminated medical product) and to prevent further transmission from such sources.
- To identify cases that may be a source of infection for others (e.g., a sexual or drug contact) and to prevent further disease transmission from such sources.
- To identify contacts and recommend appropriate preventive measures, including hepatitis B immune globulin (HBIG) and immunization.
- To prevent transmission to children born to HBsAg + women.
- To better understand the epidemiology of HBV and the burden of morbidity from chronic infection.

Reporting requirements

- Health care providers:
  - Acute HBV: **notifiable to Local Health Jurisdiction within 3 work days**
  - Chronic HBV (initial infection only): notifiable to Local Health Jurisdiction within 1 month
  - HBV surface antigen + pregnant women: notifiable to Local Health Jurisdiction within 3 work days
- Hospitals:
  - Acute HBV: **notifiable to Local Health Jurisdiction within 3 work days**
  - Chronic HBV (initial infection only): notifiable to Local Health Jurisdiction within 1 month
  - HBV surface antigen + pregnant women: notifiable to Local Health Jurisdiction within 3 work days
- Laboratories: no requirements for reporting

- Local health jurisdictions: notifiable to DOH within 7 days of case investigation completion or summary information required within 21 days –
    - Acute HBV: Communicable Disease Epidemiology
    - Chronic HBV: Infectious Disease and Reproductive Health
    - HBV surface antigen + pregnant women: Immunization Program

CASE DEFINITION FOR SURVEILLANCE

ACUTE HEPATITIS B

Clinical criteria for diagnosis

An acute illness with:

- discrete onset of symptoms (e.g., fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), and
- jaundice or elevated serum aminotransferase levels.

Laboratory criteria for diagnosis

- Immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc) positive (preferred) or
- Hepatitis B surface antigen (HBsAg) positive, if IgM anti-HBc not done.

Case definition

- Confirmed: A case that meets the clinical criteria and is IgM anti-HBc positive

CHRONIC HEPATITIS B

Clinical criteria for diagnosis

Most HBV-infected persons are asymptomatic. However, many have chronic liver disease, which can range from mild to severe including cirrhosis, and/or liver cancer.

Laboratory criteria for diagnosis

- HBsAg positive, total anti-HBc positive and IgM anti-HBc negative, or
- HBsAg positive two times at least 6 months apart.

Case definition

All positive HBsAg test results should be followed-up to determine if the person has chronic HBV infection (see case definition above). Particular efforts should be made to follow-up women of reproductive age.

HEPATITIS B SURFACE ANTIGEN + PREGNANT WOMEN

Clinical criteria for diagnosis

Most HBV-infected persons are asymptomatic. However, many have chronic liver disease, which can range from mild to severe including cirrhosis, and/or liver cancer. Most pregnant woman with chronic HBV infection will be asymptomatic or have only mild liver disease.

Laboratory criteria for diagnosis

- HBsAg positive, total anti-HBc positive and IgM anti-HBc negative, and
- A positive pregnancy test.

Case definition

- Confirmed: A case that meets the clinical case definition and is laboratory confirmed.

A. DESCRIPTION

1. Identification

Only a small proportion of acute hepatitis B virus (HBV) infections may be clinically recognized; less than 10% of children and 30%-50% of adults with acute hepatitis B virus (HBV) infection will have icteric disease. In those with clinical illness, the onset is usually insidious, with anorexia, vague abdominal discomfort, nausea and vomiting, sometimes arthralgias and rash, often progressing to jaundice. Fever may be absent or mild. Severity ranges from inapparent cases detectable only by liver function tests to fulminating, fatal cases of acute hepatic necrosis. The case-fatality rate in hospitalized patients is about 1%; higher in those over 40 years of age. Fulminant HBV infection is also seen in pregnancy and among newborns of infected mothers.

Chronic HBV infection is found in 0.5% of adults in North America and in 0.1%-20% of people from other parts of the world. After acute HBV infection, the risk of developing chronic infection varies inversely with age; chronic HBV infection occurs among about 90% of infants infected at birth, 20%-50% of children infected at 1-5 years of age, and about 1%-10% of persons infected as older children and adults. Chronic HBV infection is also common in persons with immunodeficiency. Persons with chronic infection may or may not have a history of clinical hepatitis. About one third have an elevated aminotransferase; biopsy findings range from normal to chronic active hepatitis, with or without cirrhosis. The prognosis of liver disease in such individuals is variable. An estimated 15%-25% of persons with chronic HBV infection will die prematurely of either cirrhosis or hepatocellular carcinoma. HBV may be the cause of up to 80% of all cases of hepatocellular carcinoma worldwide, second only to tobacco among known human carcinogens.

Diagnosis is confirmed by demonstration in sera of specific antigens and/or antibodies. Three clinically useful antigen-antibody systems have been identified for hepatitis B: 1) hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs); 2) hepatitis B core antigen (HBcAg) and antibody to HBcAg (anti-HBc); and 3) hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe). Commercial kits (RIA and ELISA) are available for all markers except HBcAg. HBsAg can be detected in the serum from several weeks before onset of symptoms to days, weeks or months after onset; it persists in chronic infections. Anti-HBc appears at the onset of illness and persists indefinitely. Demonstration of anti-HBc in serum indicates HBV infection, current or past; IgM anti-HBc is present in high titer during acute infection and usually disappears within 6 months, although it can persist in some cases of chronic hepatitis; thus, this test may reliably diagnose acute HBV infection. HBsAg is present in serum during acute infections and persists in chronic infections. The presence of HBsAg indicates that the person is potentially infectious. The presence of HBeAg is associated with relatively high infectivity.

2. Infectious Agent

The hepatitis B virus (HBV), a hepadnavirus, is a 42-nm partially double-stranded DNA virus composed of a 27-nm nucleocapsid core (HBcAg), surrounded by an outer lipoprotein coat containing the surface antigen (HBsAg). HBsAg is antigenically heterogeneous, with a common antigen designated a, and two pairs of mutually exclusive antigens, d and y, and w (including several subdeterminants) and r, resulting in 4 major subtypes: adw, ayw, adr and ayr. The distribution of subtypes varies geographically; because of the common a determinant, protection against one subtype appears to confer protection against the other subtypes, and no differences in clinical features have been related to subtype.

3. Worldwide Occurrence

Worldwide; endemic with little seasonal variation. WHO estimates that more than 2 billion persons (including 350 million who are chronically infected) have been infected with HBV. Each year about a million persons die as a result of HBV infections and over 4 million new acute clinical cases occur. In countries where HBV is highly endemic (HBsAg prevalence 8% or higher), most infections occur during infancy and early childhood. In countries where HBV is intermediately endemic (HBsAg prevalence ranges from 2%-7%), infections occur commonly in all age groups, although the high rate of chronic infection is primarily maintained by transmission during infancy and early childhood. In countries with low endemicity (HBsAg prevalence less than 2%), most infections occur in young adults, especially among persons who belong to known risk groups. However, even in countries with low HBV endemicity, a high proportion of chronic infections may be acquired during childhood because the development of chronic infection is age dependent. Most of these infections would not be prevented by perinatal hepatitis B prevention programs because they occur among children of HBsAg negative mothers.

In the US and Canada, serologic evidence of previous infection varies depending on age and socioeconomic class. Overall, 5% of the adult US population has anti-HBc, and 0.5% are HBsAg positive. Exposure to HBV may be common in certain high risk groups,

including injecting drug users, heterosexuals with multiple partners, men who have sex with men, household contacts and sex partners of HBV infected persons, health care and public safety workers who have exposure to blood in the workplace, clients and staff in institutions for the developmentally disabled, hemodialysis patients and inmates of correctional facilities.

In the past, recipients of blood products were at high risk. In the many countries in which pretransfusion screening of blood for HBsAg has been required, and where pooled blood clotting factors (especially antihemophilic factor) are processed to destroy the virus, this risk has been virtually eliminated. However, this risk is still present in many developing countries. Contaminated and inadequately sterilized syringes and needles have resulted in outbreaks of hepatitis B among patients in clinics and physicians' offices; this has been a major mode of transmission worldwide. Occasionally, outbreaks have been traced to tattoo parlors and acupuncturists. Rarely, transmission to patients from HBsAg positive health care workers has been documented. A number of outbreaks occurred among patients in dialysis centers in the US due to failure to adhere to recommended infection control practices for preventing transmission of HBV and other bloodborne pathogens in these settings.

4. Reservoir

Humans. Chimpanzees are susceptible, but an animal reservoir in nature has not been recognized. Closely related hepadnaviruses have been found in woodchucks, ducks and other animals; none cause disease in humans.

5. Mode of Transmission

Body substances capable of transmitting HBV include: blood and blood products; saliva; cerebrospinal fluid; peritoneal, pleural, pericardial and synovial fluid; amniotic fluid; semen and vaginal secretions and any other body fluid containing blood; and unfixed tissues and organs. The presence of e antigen or viral DNA indicates high virus titer and higher infectivity of these fluids.

Transmission occurs by percutaneous (IV, IM, SC or intradermal) and permucosal exposure to infective body fluids. Because HBV is stable on environmental surfaces for at least 7 days, indirect inoculation of HBV can also occur via inanimate objects. Fecal-oral or vectorborne transmission has not been demonstrated.

Major modes of HBV transmission include sexual or household contact with an infected person, perinatal transmission from mother to infant, injecting drug use and nosocomial exposure. Sexual transmission from infected men to women is about three times more efficient than that from infected women to men. Anal intercourse, insertive and receptive, is associated with an increased risk of infection. Transmission of HBV in households primarily occurs from child to child. Communally used razors and toothbrushes have been implicated as occasional vehicles of HBV transmission in this setting. Perinatal transmission is common, especially when HBV infected mothers are also HBeAg positive. The rate of

transmission from HBsAg positive, HBeAg positive mothers is more than 70%, and the rate of transmission from HBsAg positive, HBeAg negative mothers is less than 10%. Transmission associated with injecting drug use can occur though transfer of HBV infected blood by sharing syringes and needles either directly or through contamination of drug preparation equipment. Nosocomial exposures that have resulted in HBV transmission include transfusion of blood or blood products, hemodialysis, acupuncture and needlesticks or other injuries from sharp instruments sustained by hospital personnel. IG, heat treated plasma protein fraction, albumin and fibrinolysin are considered safe.

6. Incubation period

Usually 45-180 days, average 60-90 days. As short as 2 weeks to the appearance of HBsAg, and rarely as long as 6-9 months; the variation is related in part to the amount of virus in the inoculum, the mode of transmission and host factors.

7. Period of communicability

All persons who are HBsAg positive are potentially infectious. Blood from experimentally inoculated volunteers has been shown to be infective many weeks before the onset of first symptoms and to remain infective through the acute clinical course of the disease. The infectivity of chronically infected individuals varies from highly infectious (HBeAg positive) to sparingly infectious (anti-HBe positive).

8. Susceptibility and resistance

Susceptibility is general. Usually the disease is milder and often anicteric in children; in infants it is usually asymptomatic. Protective immunity follows infection if antibody to HBsAg (anti-HBs) develops and HBsAg is negative. Persons with Down syndrome, lymphoproliferative disease, HIV infection and those on hemodialysis appear to be more likely to develop chronic infection.

B. METHODS OF CONTROL

1. Preventive measures:

a. Effective hepatitis B vaccines have been available since 1982. Two types of hepatitis B vaccines have been licensed in the US and Canada. Both have been shown to be safe and highly protective against all subtypes of HBV. The first type is prepared from plasma from HBsAg positive persons; it is no longer produced in the US but is still used widely elsewhere. The second type is made by recombinant DNA (rDNA) technology; it is produced by using HBsAg synthesized by Saccharomyces cerevisiae (common baker's yeast) into which a plasmid containing the gene for HBsAg has been inserted. Combined passive-active immunoprophylaxis with hepatitis B immunoglobulin (HBIG) and vaccine has been shown to stimulate anti-HBs titers comparable to vaccine alone.

i. In all countries, routine infant immunization should be the primary strategy to prevent HBV infection. Immunization of successive infant cohorts should produce a highly immune population sufficient to interrupt transmission. In countries with high endemicity of HBV infection, routine infant immunization will rapidly eliminate transmission because virtually all chronic infections are acquired among young children. In countries with intermediate and low HBV endemicity, immunizing infants alone will not substantially lower disease incidence because most infections occur among adolescents and young adults. In these countries, vaccine strategies for older children, adolescents and adults may be desirable. Strategies to ensure high vaccine coverage of successive age group cohorts are likely to be most effective in eliminating HBV transmission. In addition, immunization strategies can be targeted to high risk groups, which account for most cases among adolescents and adults.

ii. Testing to exclude people with preexisting anti-HBs or anti-HBc is not required prior to immunization, but may be desirable as a cost saving method where there is a high level of preexisting infection.

iii. Immunity against HBV is believed to persist for at least 15 years after successful immunization.

iv. Vaccines licensed in different parts of the world may have varying dosages and schedules; the vaccines currently licensed in the US are most commonly administered in 3 IM doses: an initial dose with subsequent doses 1 to 2 and 6 to 18 months later; for infants, the first dose is given at birth or at 1-2 months of age. For infants born to HBsAg positive women, the schedule should be birth, 1-2 and 6 months of age. These infants should also receive 0.5 ml of HBIG (see B2ei, below). The dose of vaccine varies by manufacturer; the package insert should be consulted. In mid 1999, it was announced that very small infants who receive multiple doses of vaccines containing thimerosal could receive more than the recommended limits for mercury exposure based on recently developed guidelines. Reduction or elimination of thimerosal in vaccines as rapidly as possible was encouraged. As of mid 1999, several of the available inactivated vaccines and all live vaccines were thimerosal free. As of mid 1999, only hepatitis B vaccines that were approved for use at birth contained thimerosal. Therefore, it was recommended that hepatitis B immunization be delayed until 2-6 months of age for infants born to hepatitis B surface antigen negative mothers unless hepatitis B vaccines that do not contain thimerosal are available. For infants born to HBsAG positive mothers and mothers who were not screened during pregnancy, the recommendations were unchanged and called for administration of vaccine at birth. Single antigen preservative free hepatitis B vaccine became available in the US in mid September 1999.

v. Pregnancy is not a contraindication for receiving hepatitis B vaccine.

b. The current hepatitis B prevention strategy in the US includes the following components: a) screening of all pregnant women for the presence of HBsAg, providing HBIG and hepatitis B vaccine to infants of HBsAg positive mothers, and providing hepatitis B vaccine to susceptible household contacts (see B2e, below); b)

providing routine hepatitis B immunization for all infants; c) providing catch-up immunization to children who are in groups with high rates of chronic HBV infection (Alaskan natives, Pacific Islanders and children of first generation immigrants from countries with a high prevalence of chronic HBV infection); d) catch-up immunization of previously unimmunized children and adolescents, with the highest priority children aged 11-12 years; and e) intensified efforts to immunize adolescents and adults in defined risk groups (see B1c, next below).

c. Persons at high risk who should routinely receive preexposure hepatitis B immunization include the following: a) sexually active heterosexual men and women, including those who are diagnosed as having recently acquired other STDs, and people who have a history of sexual activity with more than one partner in the previous 6 months; b) men who have sex with men; c) sexual partners and household contacts of HBsAg positive persons; d) inmates of correctional facilities, including juvenile detention facilities, prisons and jails; e) healthcare and public safety workers who perform tasks involving contact with blood or blood contaminated body fluids; f) clients and staff of institutions for the developmentally disabled; g) hemodialysis patients; h) patients with bleeding disorders who receive blood products; and i) international travelers who plan to spend more than 6 months in areas with intermediate to high rates of chronic HBV infection (2% or greater) and who will have close contact with the local population.
d. Adequately sterilize all syringes and needles (including acupuncture needles) and stylets for finger puncture, or preferably use disposable equipment whenever possible. A sterile syringe and needle are essential for each individual receiving skin tests, other parenteral inoculations or venipuncture. Discourage tattooing; enforce aseptic sanitary practices in tattoo parlors.
e. In blood banks, all donated blood should be tested for HBsAg by sensitive tests (RIA or EIA); reject as donors all persons with a history of viral hepatitis, those who have a history of injecting drug use or show evidence of drug addiction or those who have received a blood transfusion or tattoo within the preceding 6 months. Use paid donors only in emergencies.
f. Limit administration of unscreened whole blood or potentially hazardous blood products to those patients in clear and immediate need of such therapeutic measures.
g. Maintain surveillance for all cases of posttransfusion hepatitis, keep a register of all people who donated blood for each case. Notify blood banks of these potential carriers so that future donations may be identified promptly.
h. Medical and dental personnel who are infected with HBV and are HBeAg positive should not perform invasive procedures unless they have sought counsel from an expert review panel and have been advised under what circumstances, if any, they may continue to perform these procedures.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Universal precautions to prevent exposures to blood and body fluids.

c. Concurrent disinfection: Of equipment contaminated with blood or infectious body fluids.
d. Quarantine: None.
e. Immunization of contacts: Products available for postexposure prophylaxis include HBIG and hepatitis B vaccine. HBIG has high titers of anti-HBs (more than 1:100,000). When indicated, it is important to administer HBIG as soon after exposure as possible.
    i. Infants born to HBsAg positive mothers should be given a single dose of HBIG (0.5 ml IM) and vaccine within 12 hours of birth. The first dose of vaccine should be given concurrently with HBIG at birth but at a separate site. The second and third doses of vaccine (without HBIG) are given 1-2 and 6 months later. It is recommended to test the infant for HBsAg and anti-HBs at 9-15 months of age to monitor the success or failure of therapy. Infants who are anti-HBs positive and HBsAg negative are protected and do not need further vaccine doses. Infants found to be anti-HBs negative and HBsAg negative should be reimmunized.
    ii. After percutaneous (e.g., needle stick) or mucous membrane exposures to blood that contains or might contain HBsAg, a decision to provide postexposure prophylaxis must include consideration of several factors: i) whether the source of the blood is available; ii) the HBsAg status of the source; and iii) the hepatitis B immunization status of the exposed person. For previously unimmunized persons exposed to blood from an HBsAg positive source, a single dose of HBIG (0.06 ml/kg, or 5 ml for adults) should be given as soon as possible, but at least within 24 hours after high risk needle stick exposure, and the hepatitis B vaccine series should be started. If active immunization cannot be given, a second dose of HBIG should be given 1 month after the first. HBIG is not usually given for needle stick exposure to blood that is not known or highly suspected to be positive for HBsAg, since the risk of infection in these instances is small; however, initiation of hepatitis B immunization is recommended if the person had not previously been immunized. For previously immunized persons exposed to an HBsAg positive source, postexposure prophylaxis is not needed for persons who had a protective antibody response to immunization (anti-HBs titer of 10 milli-IUs/ml or greater). For persons whose response to immunization is unknown, hepatitis B vaccine and/or HBIG should be administered.
    iii. After sexual exposure to a person with acute HBV infection, a single dose of HBIG (0.06 ml/kg) is recommended if it can be given within 14 days of the last sexual contact. For all exposed sexual contacts of persons with acute and chronic HBV infection, vaccine should be administered.
f. Investigation of contacts and source of infection: See B3, below.
g. Specific treatment: No specific treatment is available for acute hepatitis B. Alpha interferon and lamivudine have been licensed for treatment of chronic hepatitis B in the US. Candidates for therapy should have liver biopsy evidence of chronic hepatitis B; treatment is most effective in individuals in the high-replicative phase (HBeAg positive) of infection because they are the most likely to be symptomatic, infectious and at greatest risk of long-term sequelae. Studies have shown that alpha

interferon is successful in arresting viral replication in about 25%-40% of treated patients. Approximately 10% of patients who respond lose HBsAg 6 months after therapy. Clinical trials of long-term treatment with lamivudine have demonstrated sustained clearance of HBV DNA from serum, followed by improvements in serum aminotransferase levels and histologic improvement.

3. Epidemic measures

When two or more cases occur in association with some common exposure, conduct a search for additional cases. Institute strict aseptic techniques. If a plasma derivative such as antihemophilic factor, fibrinogen, pooled plasma or thrombin is implicated, withdraw the lot from use and trace all recipients of the same lot in a search for additional cases.

4. International measures

None.